Remarks

Claims 1-10 were pending in the subject application. By this Amendment claims 1, 2, 5 and 8 have been amended, claims 9 and 10 have been cancelled, and claims 11-18 have been added. Thus, claims 1-8 and 11-18 are now presented for consideration by the Examiner.

Support for these amendments and new claims can be found throughout the subject specification. The amendments to the claims have been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. These amendments should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Claims 1-5 have been rejected under 35 U.S.C. §112, first paragraph. The applicant respectfully traverses this grounds for rejection because a person skilled in the art, having the benefit of the applicant's disclosure, could practice the full scope of the invention as set forth in the presently-amended claims.

A central aspect of the subject invention is the recognition that the acid resistance of an antibody is an indication of its high affinity properties. There is no reason to believe that the significance of acid resistance with respect to high affinity depends upon the antigen to which the antibody is raised, or the animal in which the antibody is raised. Thus, although a particular example is provided in the current application, namely sheep antibodies to the CEA antigen, the methodology, which is clearly described in the application can be applied to other naturally occurring antibodies as a means of providing antibodies with high affinity.

It should be noted that the requirement for some experimentation and/or screening does not necessarily make a claim non-enabled. "Enablement is not precluded by the necessity for some experimentation such as routine screening. A considerable amount of experimentation is permissible, if it is merely routine . . ." (emphasis added). *In re Wands*, 8 USPQ 2d 1400, 1404 (Fed. Cir. 1988). In the current case, any experimentation needed to identify antibodies having the specified activity would be routine given the guidance provided in the subject application. This guidance includes the identification of a specific testing protocol as well as methods of raising antibodies.

The applicants respectfully submit that, to limit their patent coverage to the one specific antibody, would essentially eviscerate their patent protection. Others skilled in the art and having the benefit of the current disclosure, could, with minimal effort, readily prepare and identify other antibodies having the advantageous high binding affinity.

The Federal Circuit's predecessor, the Court of Customs and Patent Appeals (CCPA), has directly addressed the issue of claim scope. In addressing the enablement of relatively broad claims the CCPA noted:

> What were once referred to as "basic inventions" have led to "basic patents," which amounted to real incentives, not only to invention and its disclosure, but to its prompt, early disclosure. . . .See *In re Goffe, 542 F.2d 564, 191 USPQ 429 (CCPA 1976)*. (emphasis added).

It is important to bear in mind that for an invention to be enabled under the first paragraph of 35 U.S.C. §112, the specification need only teach a person of ordinary skill in the art "how to make" and "how to use" the invention. It is further noted that the sheer number of compounds that may fall within the scope of a claim is not determinative of the enablement of the specification. See, e.g., *In re Angstadt*, 537 F.2d 498, 190 USPQ 214 (CCPA 1976), where the court observed that a large list of materials, in combination with a teaching of how to carry out the invention, was enabling for purposes of §112.

The applicants are cognizant of their duty under 35 U.S.C. §112, first paragraph, to provide sufficient teaching in the specification to enable one skilled in the art to practice the invention as claimed without undue experimentation. For the reasons set forth above, the applicants believe that they have fulfilled that duty. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Please note that, in order to clarify the scope of the claimed invention, the claims have been amended herein to explicitly recite that the antibodies are natural (rather than mutated) antibodies and that they are raised to protein antigens (as opposed to, for example, haptens). The amended claims (and the new claims), combined with the amendments discussed below, clearly circumscribe the reasonable scope of the claimed subject matter.

Claims 2-8 have been rejected under 35 U.S.C. §112, second paragraph. The applicant appreciates the Examiner's careful review of the claims and the claims have been amended herein to address the issues raised by the Examiner.

With respect to the Examiner's rejection under §112 of claim 2, it should be clear to the skilled person that the reference in claim 2 is to the amount of antibody bound at the end of the process described in claim 1. Thus, one would proceed through all of the steps in claim 1, and determine the amount of antibody bound to antigen. At the end of Step VII of the process described in claim 1, it is stated "wherein the amount bound in the second sample is greater than 50% of that of the first sample." Thus, claim 2 is a further limitation on that step, *i.e.* that the amount of antibody bound in the second sample is greater than 60% of that bound in the first sample. In order to clarify this point, claim 2 has been amended to explicitly recite that the ">60%" refers to after step vii.

With respect to the Examiner's rejection of claim 8 under §112, a particular antibody is described, with reference to sequence information provided in the application. The claim also, however, covers a "variant." This variant must have the acid resistance properties as the antibody described by reference to the sequence information. The acid resistance properties can be determined by the methods as set out in claim 1. In other words, if one compared the antibody having the particular sequence with a variant, both such antibodies should have the same properties as determined using the methodology described in claim 1, *i.e.* measuring acid resistance. Claim 8 has been amended herein to clarify this point.

The applicant believes that, in view of the amendments set forth herein, the claims as now presented clearly delineate the metes and bounds of the claimed invention. Accordingly, the applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Claims 1-4 have been rejected under 35 U.S.C. §102(b) as being anticipated by Groves *et al.* 1987 (*Hybridoma* 6:71-76). Also, claims 1-4 have been rejected under 35 U.S.C. §102(b) as being anticipated by Groves *et al.* 1990 (*Journal of Endocrinology* 126:217-222). The applicants respectfully traverse these grounds for rejection because the antibodies disclosed in the cited references are binding to haptens as opposed to protein antigens as in the case of the antibodies of the subject invention.

Haptens (such as testerone and progesterone) are, of course, not immunogenic proteins, although they do bind to antibodies. The high affinity binding of the applicant's antibodies to protein antigens is to be distinguished from antibodies binding to haptens. Haptens are known to fit, because of their small size, into internal crevices of antibodies. Accordingly, the existence of antibodies having high affinity for hapten molecules does not anticipate the antibodies of the subject invention, which are characterized by their excellent binding affinity for protein antigens.

It is basic premise of patent law that, in order to anticipate, a single prior art reference must disclose within its four corners, each and every element of the claimed invention. In *Lindemann v. American Hoist and Derrick Co.*, 221 USPQ 481 (Fed. Cir. 1984), the court stated:

> Anticipation requires the presence in a single prior art reference, disclosure of each and every element of the claimed invention, arranged as in the claim. *Connell v. Sears Roebuck and Co.*, 722 F.2d 1542, 220 USPQ 193 (Fed. Cir. 1983); *SSIH Equip. S.A. v. USITC*, 718 F.2d 365, 216 USPQ 678 (Fed. Cir. 1983). In deciding the issue of anticipation, the [examiner] must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference. *SSIH, supra*; *Kalman [v. Kimberly-Clarke*, 713 F.2d 760, 218 USPQ 781 (Fed. Cir. 1983)] (emphasis added). 221 USPQ at 485.

In *Dewey & Almy Chem. Co. v. Mimex Co.*, Judge Learned Hand wrote:

> No doctrine of the patent law is better established than that a prior patent . . . to be an anticipation must bear within its four corners adequate directions for the practice [of the subsequent invention] . . . if the earlier disclosure offers no more than a starting point . . . if it does not inform the art without more how to practice the new invention, it has not correspondingly enriched the store of common knowledge, and it is not an anticipation. 124 F.2d 986, 990; 52 USPQ 138 (2nd Cir. 1942).

Please note that the claims have been amended to clarify that the advantageous and surprisingly high binding affinity of the antibodies of the subject invention is with respect to binding between the antibody and a protein antigen to which the antibody has been raised. The two Groves *et al.* references, which pertain to the binding of antibodies to haptens, do not disclose or suggest the applicant's claimed antibodies. Therefore, the applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. §102 based on the Grove *et al.* references.

Claims 1-4, 7 and 8 have been rejected under 35 U.S.C. §102(b) as being anticipated by Yang *et al.* 1995 (*Journal of Molecular Biology* 254:392-403); claims 1-5, 7 and 8 have been rejected under 35 U.S.C. §102(b) as being anticipated by Schier *et al.* 1996 (*Journal of Molecular Biology* 263:551-567); and claims 1-8 have been rejected under 35 U.S.C. §102(b) as being anticipated by Osbourn *et al.* 1996 (*Immunotechnology* 2:181-196). The applicant respectfully traverses this grounds for rejection because the cited references do not disclose or suggest the current applicant's high affinity natural antibodies.

The Yang *et al.*, Osbourn *et al.* and Schrier *et al.* citations all disclose antibodies which are effectively mutated antibodies. It is well known that producing antibody libraries results in mutations which in certain cases can lead to the provision of high affinity antibodies. However, such antibodies are clearly different from the antibodies disclosed in the present application which are based on "naturally occurring" antibodies. Accordingly, the applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. §102(b) based on the Yang *et al.*, Osbourn *et al.* and Schrier *et al.* references.

Claims 1-6 have been rejected under 35 U.S.C. §102(b) as being anticipated by Buchegger *et al.* 1987 (*Journal of the National Cancer Institute* 79:337-342). Also, claims 1-6 have been rejected under 35 U.S.C. §102(b) as being anticipated by WO 91/01990 (Shively *et al.*). The applicant respectfully traverses this grounds for rejection because the cited references do not disclose "high affinity" antibodies as contemplated and claimed in the current application.

With respect to the Buchegger *et al.* and Shively *et al.* references, the antibodies disclosed therein are not, as a skilled person would understand it, "high affinity" antibodies. Given the affinity values quoted in those citations, the skilled person would immediately recognize they do not fall within the scope of the claims of the present application because they do not meet the necessary criteria of being "high affinity."

It should also be noted that there is no reason to believe that the antibodies of the cited references possess the acid stability that is critical to the subject invention.

The applicant respectfully points out that for a claim to be anticipated under the principles of inherency, the subject of a single prior art reference must necessarily possess the limitations of that which is now claimed. *In re King*, 801 F2d 1324, 1326, 231 USPQ 136, 138 (Fed. Cir. 1986). Further,

> the doctrine of inherency is available only when the prior inherent event can be established as a certainty. That an event may result from a given set of circumstances is not sufficient to establish anticipation. . . . A prior inherent event cannot be established based on speculation, or where a doubt exists (emphasis added). *Ethyl Molded Product Co. v. Betts Package Inc.*, 9 USPQ 2d 1001, 1032-33 (E.D. KY 1988).

The claims of the subject application are directed to antibodies having very specific advantageous properties. Under the authority of *In re King*, for the cited references to be an effective basis for a rejection under 35 U.S.C. §102, the disclosed antibodies must possess the characteristics of the applicant's claimed antibodies. Such characteristics must be a certainty. It cannot be based on speculation or probabilities. It is by no means a certainty, and in fact, as discussed above, it is doubtful, that the antibodies of the cited references have the characteristics of the applicant's claimed antibodies.

Accordingly, the applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. §102(b) based on the Buchegger *et al.* and Shively *et al.* references.

Claims 1-8 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14, 19 and 22-24 of co-pending Application No. 09/786,013. The applicants respectfully acknowledge the double patenting rejection and, upon an indication of allowable subject matter in the current application, will conduct a review of the claims (if any) pending at that time in the 09/786,013 application. To the extent that an issue of double patenting exists at that time, the applicants will file a Terminal Disclaimer.

In view of the foregoing remarks and the amendments above, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicant also invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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